REMARKS

Claims 51 and 53-60 were pending in the subject application. By this Amendment, applicants have amended claims 51 and 57, and canceled claims 53-56 and 58-60. Applicants maintain that no issue of new matter is raised by these amendments. Upon entry of this Amendment, claims 51 and 57 will be pending and under examination.

Obviousness-Type Double Patenting Rejection

On page 2 of the May 31, 2007 Office Action, the Examiner maintained the provisional rejection of previously pending claims 51 and 53-58 as allegedly unpatentable on the ground of nonstatutory obviousness-type double patenting over claims 1-5, 18 and 31 of U.S. Serial No. 10/371,483.

In response, applicants respectfully traverse this obviousness-type double patenting rejection. Applicants note that U.S. Serial No. 10/371,483 is now U.S. Patent No. 7,122,185, issued October 17, 2006. Without conceding the correctness of the Examiner's position, applicants maintain that if upon entry of this Amendment the pending claims are otherwise deemed allowable, applicants will consider filing a Terminal Disclaimer.

Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 57-60 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. Specifically, the Examiner stated that neither the specification nor the prior art disclose any real *in vivo* or *in vitro* data to show any anti-CCR5 antibody as an effective medicine.

In response, applicants submit that the skilled practitioner in the art would know how to use a pharmaceutical composition comprising CCR5 antibodies to inhibit HIV-1 infection of a CD4+ cell without undue experimentation. Without conceding the correctness of the Examiner's

ground of rejection, applicants have canceled claims 58-60 and amended claims 57 to recite a "composition comprising the antibody" of claim 57 "and a carrier", thereby obviating the Examiner's ground of rejection. Accordingly, applicants maintain that claim 57 as amended complies with the enablement requirement of 35 U.S.C. §112, first paragraph, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection Under 35 U.S.C. §102/§103

The Examiner rejected claims 51 and 53-60 under 35 U.S.C. §102(e) as anticipated by, or in the alternative, under 35 U.S.C. §103 as obvious over Li et al. (US 6,759,519) as evidenced by Wu et al. (US 6,528,625). Specifically, the Examiner alleged that Li et al. disclose an antibody which binds to a polypeptide designated HDGNR10 whose sequence is identical to that of CCR5. The Examiner also alleged that although Li et al. do not disclose that anti-HDGNR10 antibodies can block HIV entry into cells, it is expected that at least one of the polyclonal antibodies disclosed in Li et al. should possess the same characteristics as that of the claimed antibody. The Examiner further alleged that Li et al. teach an isolated antibody that binds to an extracellular portion of HDGNR10 and is an antagonist of the HDGNR10 polypeptide. The Examiner alleged that this isolated antibody appears to have the same characteristics as the anti-CCR5 antibody disclosed by Wu et al. The Examiner stated that Wu et al. disclose the monoclonal antibody 2D7 which specifically binds to the second extracellular loop of CCR5, inhibits HIV entry and chemotaxis of CCR5 in response to RANTES, MIP1α and MIP1β. Thus, the Examiner alleged that the claimed antibodies appear to be the same or obvious variations of the antibodies disclosed in the prior art absent a showing of unobvious differences.

In response, applicants respectfully traverse the Examiner's ground of rejection. Applicants note that claims 53-56 and 58-60 have been canceled rendering moot the Examiner's ground of rejection as to these claims.

Applicants' invention as recited in presently amended claim 51 is an isolated monoclonal antibody which binds to a human CCR5 chemokine receptor on the surface of a CD4+ cell, wherein the antibody inhibits fusion of HIV-1, or an HIV-1 infected cell, to the CD4+ cell, so as to thereby inhibit HIV-1 infection of the CD4+ cell, wherein the CD4+ cell may be any of a PM-1 cell, a primary CD4+ T-cell, or a peripheral blood mononuclear cell (PBMC).

Li et al. disclose the polypeptide designated HDGNR10 whose amino acid sequence is highly homologous to that of human CCR5. In column 12, lines 20-27, Li et al. generally disclose that "an antibody may antagonize a G-protein chemokine receptor of the present invention, or in some cases an oligopeptide, which binds to the G-protein chemokine receptor but does not elicit a second messenger response such that the activity of the G-protein chemokine receptors is prevented." In column 18, lines 6-7, Li et al. state that "[t]hese antibodies can be, for example, polyclonal or monoclonal antibodies." In column 18, lines 13-14, Li et al. generally state that "an antibody generated against the chemokine receptor may agonize or may antagonize the chemokine receptor." Li et al. further disclose in column 18, lines 15-21, that "antibodies generated against the polypeptides corresponding a sequence of the present invention can be obtained by direct injection of the polypeptides into an animal or by administering the polypeptides to an animal, preferably a nonhuman. The antibody so obtained will then bind to the polypeptides itself." In column 18, lines 23-24, Li et al. also state that "[s]uch antibodies can then be used to isolate the polypeptide from tissue expressing that polypeptide."

Li et al. merely teach a broad genus of antibodies generated against isolated HDGNR10 (CCR5 receptor) polypeptide, and that the antibodies will bind HDGNR10. Li et al. do not disclose any specific antibody, let alone how to make any antibody within this broad genus which has the properties recited in amended claim 51. Although Wu et al. disclose a specific anti-CCR5 antibody 2D7 which binds to the second

extracellular loop of CCR5 on the surface of a cell, Wu et al. is not prior art as to the subject application and there is no nexus between the broad genus of Li et al. and the specific antibody of Wu et al.

Rejection Under 35 U.S.C. §102(e)

Li et al. do not disclose an isolated monoclonal anti-CCR5 antibody which (a) binds to CCR5 on the surface of a cell, and (b) inhibits fusion of HIV-1 or an HIV-1 infected cell to any of the CD4+ cells enumerated in amended claim 51. The broad genus of antibodies disclosed by Li et al. are generated against an isolated HDGNR10 polypeptide or fragments of such polypeptide. In contrast, applicants' claimed monoclonal antibody binds to a CCR5 receptor on the surface of a CD4+ cell, i.e. to a CCR5 receptor folded in a tertiary structure compatible with being part of the membrane surface of a CD4+ cell in such a way to inhibit fusion of the CD4+ cell and HIV or HIV-infected cell.

Li et al. do not disclose that any anti-HDGNR10 antibody can block HIV entry into cells, and certainly do not suggest or disclose that the entire genus of antibodies disclosed can do so. Indeed, Li et al. do not disclose any connection between the CCR5 chemokine receptor and HIV entry into a cell, or refer to HIV at all. In contrast, applicants' claimed antibody inhibits fusion of HIV-1, or an HIV-1 infected cell, to specific enumerated CD4+ cells, so as to thereby inhibit HIV-1 infection of the CD4+ cell.

On page 5 of the May 31, 2007 Office Action, the Examiner alleges that Wu et al. provides evidence that Li's antibodies "appear" to have the same characteristics as that of anti-CCR5 antibodies that block HIV fusion, and that the antibodies of Li et al. "should possess" such property of blocking HIV fusion to CD4+ cells because Li et al.'s polyclonal antibodies contain many antibodies that specifically bind to different epitopes of HDGNR10, at least one of which "would be expected" to have the claimed properties.

As an initial matter, applicants' point out that amended claim 51 is directed to an isolated monoclonal antibody. Therefore, the properties present in any polyclonal antibody disclosed by Li et al. is not relevant to whether Li et al. anticipates applicants amended claim 51, which it does not do so.

Applicants further note that to the extent the Examiner is attempting to base the rejection over Li et al. on "inherency", "[t]he fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. See M.P.E.P. §2112 citing *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). 'To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'' *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999)." In addition, "[a]n invitation to investigate is not an inherent disclosure" where a prior art reference "discloses no more than a broad genus of potential applications of its discoveries." *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1367, 71 USPQ2d 1081, 1091 (Fed. Cir. 2004).

Applicants maintain that, contrary to the Examiner's rationale, Li et al.'s broad disclosure of antibodies that bind to HDGNR10 polypeptides which can be agonists or antagonists is not an inherent disclosure of applicants' claimed antibody.

Li et al. do not remotely teach anti-CCR5 receptor antibodies capable inhibiting fusion of specific CD4+ cells and HIV-1 (or HIV-1 infected cells), let alone ones which can inhibit infection of such cells by

HIV-1. In this regard, Wu et al. do not disclose any anti-CCR5 antibodies disclosed in Li et al. and therefore is not evidence that Li et al.'s genus of antibodies can inhibit HIV-1 fusion to CD4+ cells, or inhibit HIV-1 infection of such cells.

Applicants further maintain that not all antibodies which bind to the CCR5 receptor also inhibit fusion of a CD4+ cells and HIV-1 or an HIV-1 infected cell. Accordingly, the inhibition of fusion of HIV-1 to a CD4+ cell thereby inhibiting HIV-1 infection of such cell is not an inherent property of anti-CCR5 antibodies. As evidence, applicants submit attached as **Exhibit 1** hereto, Vila-Coro et al., (2000) *PNAS* 97(7):3388-3393 which discloses anti-CCR5 monoclonal antibody CCR5-02 which was produced against the CCR5 extracellular domain. Vila-Coro et al. discuss on page 3392 that certain anti-CCR5 monoclonal antibodies are unable to block HIV-1 infection (See page 3392, first column, last paragraph, to second column first paragraph). Applicants also submit attached as **Exhibit 2** hereto, Lee et al., (1999) *J. Biol. Chem.* 274(14):9617-9626 which discloses that the ability of an anti-CCR5 monoclonal antibody to inhibit fusion of HIV-1 to a CD4+ cell, e.g. a PM1 cell, does not accurately predict virus neutralization activity. Specifically, Lee et al. tested multiple anti-CCR5 monoclonal antibodies generated to the extracellular domains of CCR5 including monoclonal antibody 2D7 and found that none of the other anti-CCR5 monoclonal antibodies other than 2D7 consistently blocked HIV infection. (See page 9621, second column).

Accordingly, applicants maintain that Li et al. do not disclose applicants' claimed antibodies. Applicants maintain that claims 51 and 57 as amended are not anticipated by Li et al. and respectfully request that the Examiner reconsider and withdraw this ground of rejection under 35 U.S.C. §102(e).

Rejection Under 35 U.S.C. §103

As stated above, Li et al. do not disclose an isolated monoclonal anti-CCR5 antibody which (a) binds to CCR5 on the surface of a cell, and (b) inhibits fusion of HIV-1 or an HIV-1 infected cell to any of

the CD4+ cells enumerated in amended claim 51. The broad genus of antibodies disclosed by Li et al. are generated against an isolated HDGNR10 polypeptide or fragments of such polypeptide. In contrast, applicants' claimed monoclonal antibody binds to a CCR5 receptor on the surface of a CD4+ cell, i.e. to a CCR5 receptor folded in a tertiary structure compatible with being part of the membrane surface of a CD4+ cell in such a way to inhibit fusion of the CD4+ cell and HIV or HIV-infected cell.

Li et al. do not disclose that any anti-HDGNR10 antibody can block HIV entry into cells, and certainly do not suggest or disclose that the entire genus of antibodies disclosed can do so. Indeed, Li et al. do not disclose any connection between the CCR5 chemokine receptor and HIV entry into a cell, or refer to HIV at all. In contrast, applicants' claimed antibody inhibits fusion of HIV-1, or an HIV-1 infected cell, to specific enumerated CD4+ cells, so as to thereby inhibit HIV-1 infection of the CD4+ cell.

Applicant notes that obviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established. See M.P.E.P. §2141.02(V) citing *In Re Rijckaert*, 9 F.2d 1531, 28 USPQ2d 1955 (Fed. Cir. 1993). Accordingly, applicants maintain that Wu et al. cannot be used in rejecting claims 51 and 57 as obvious in light of the disclosure of Li et al. under 35 U.S.C. §103. Applicants therefore maintain that as discussed above, Li et al. do not teach each and every element of the claimed antibodies which are therefore not obvious over Li et al.

In view of the remarks above, applicants maintain that the claimed antibodies as recited in amended claims 51 and 57 are not rendered obvious by the disclosure of Li et al. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection Under 35 U.S.C. §103

The Examiner rejected claims 51 and 53-60 under 35 U.S.C. §103 as allegedly obvious over Cocchi et al. and Samson et al. in view of Berger et al. (US 6,197,578). Specifically, the Examiner alleged that although neither Cocchi et al. nor Samson et al. teach any antibody against CCR5 that can inhibit HIV infection, Berger et al. teaches that CXCR4 on the surface of CD4+ cells is associated with HIV fusion and that anti-CXCR4 antibodies can block fusion of HIV to a CD4+ cell. The Examiner also alleged that Berger et al. teach how to generate antibodies against chemokine receptors and suggests the use of such antibodies in pharmaceutical compositions. The Examiner therefore alleged that, based on an analogy to the anti-CXCR4 antibodies, it would have been obvious to one skilled in the art to make antibodies against CCR5 in order to inhibit HIV fusion to CD4+ cells.

In response, applicants respectfully traverse the Examiner's ground of rejection. Applicants note that claims 53-56, 58 and 60 have been canceled rendering moot the Examiner's ground of rejection as to these claims.

Applicants' invention as recited in presently amended claim 51 is an isolated antibody which binds to a human CCR5 chemokine receptor on the surface of a CD4+ cell, wherein the antibody inhibits fusion of HIV-1, or an HIV-1 infected cell, to the CD4+ cell, so as to thereby inhibit HIV-1 infection of the CD4+ cell.

Cocchi et al. disclose that the chemokines RANTES, MIP-1α, and MIP-1β were identified as the major HIV suppressive factors produced by CD8+ cells by analyzing culture supernatants of CD8+ cell lines. These results were compared to supernatants of CD4+ cell lines, which only produced MIP-1α and MIP-1β.

Samson et al. disclose the cloning of a human gene named ChemR13, now known as CCR5, and its deduced amino acid sequence.

Berger et al. disclose the human chemokine receptor CXCR4 as a human accessory molecule associated with HIV entry into CD4+ cells and antibodies to CXCR4. CXCR4 is a known member of the superfamily of G-protein-coupled cell surface molecules and is an alpha-chemokine receptor specific for stromal-derived-factor-1 (SDF-1). T-cell tropic HIV isolates bind to CXCR4 to infect CD4+ T-cells. As disclosed in column 20, lines 20-30 and Figures 2 and 3 of Berger et al., anti-CXCR4 antibodies inhibited fusion mediated by the prototypic T-cell line-tropic LAV env, but did not inhibit fusion mediated by the prototypic macrophage-tropic Ba-L env.

As the Examiner acknowledged on page 22 of the May 31, 2007 Office Action, neither Cocchi et al. nor Samson et al. disclose any anti-CCR5 antibodies which inhibit fusion of HIV to CD4+ cells. Applicants maintain that Berger et al. also do not disclose any such antibodies. Accordingly, applicants maintain that no combination of these three references results in each and every element of the claimed antibody recited in amended claim 51.

In addition, applicants maintain that contrary to the Examiner's assertion, one skilled in the art would not have made the claimed antibodies based on the teachings of these three references. Applicants respectfully disagree with the Examiner and maintain that the anti-CXCR4 antibodies of Berger et al. are not analogous to the claimed antibodies which bind to a human CCR5 receptor on the surface of a CD4+ cell.

Based on the teachings of Berger et al., one skilled in the art would not have arrived at the claimed antibodies which, in contrast to the antibodies of Berger et al., inhibit fusion mediated by macrophage-tropic HIV-1 env, but do not inhibit fusion mediated by T-cell-tropic HIV-1 env. As disclosed in Table 3 of Example 2 on page 32 of the specification, CCR5 expression permits infection of CD4+ cells by macrophage tropic (primary NSI) HIV-1 isolates. In this example, the combination of RANTES, MIP-1α, and MIP-1β inhibited entry of the macrophage-tropic HIV strains ADA and BaL into all three CCR5-

expressing cell lines, while entry of T-cell tropic HIV HxB2 was insensitive to the β-chemokines. These results demonstrate that CCR5 functions as a second receptor for macrophage-tropic HIV strains, not for the T-cell tropic HIV strains for which CXCR4 functions as a coreceptor. Accordingly, applicants maintain that the claimed antibodies are not analogous to the antibodies of Berger et al.

Applicants maintain that it would not have been obvious to one skilled in the art from the teachings of Berger et al. that the CCR5 receptor disclosed in Samson et al. is the second receptor that permits entry of macrophage-tropic HIV strains into cells. In fact, as discussed above, this teaching is central to applicants' specification. Accordingly, applicants maintain that the disclosures of the cited references do not render obvious applicants' claimed antibodies.

In view of the remarks above, applicants maintain that the claimed antibodies as recited in amended claims 51 are not rendered obvious by Cocchi et al. and Samson et al. in view of Berger et al. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw these grounds of rejection.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

Supplemental Information Disclosure Statement

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following documents listed below which are also listed on Substitute Form PTO-1449 **(Exhibit A)**.

This Supplemental Information Disclosure Statement is being submitted pursuant to 37 C.F.R. §1.97(c) before the mailing of a Final Office Action, Notice of Allowance or an action that otherwise closes

prosecution in the application. Pursuant to 37 C.F.R. § 1.97 (c)(2), the fee set forth in § 1.17(p) must accompany this Supplemental Information Disclosure Statement. The fee set forth in § 1.17(p) is ONE HUNDRED AND EIGHTY DOLLARS ($180.00) and a check including this amount is enclosed. Thus, this Supplemental Information Disclosure Statement should be entered and considered.

In accordance with 37 C.F.R. §1.92(a)(2)(ii), copies of the U.S. Patents and U.S. Patent Application Publications listed herein are not provided. Accordingly, copies of documents listed below as items 1-8 are not submitted herewith. Copies of documents listed below as items 9-230 are attached hereto as **Exhibits 1-222**.

1. U.S. Patent No. 5,449,608 issued September 12, 1995 to Young;

2. U.S. Patent No. 7,138,119 issued November 21, 2006 to W.C. Olson et al.;

3. U.S. Patent No. 7,060,273 issued June 13, 2006 to W.C. Olson et al.;

4. U. S. Patent No. 7,122,185 issued October 17, 2006 to W.C. Olson et al.;

5. U.S. Patent No. 6,908,734 issued June 21, 2005 to T. Dragic et al.;

6. C. Combadiere et al., U.S. Patent Application Publication No. 2005-0118677 published June 2, 2005;

7. W.C. Olson et al., U.S. Patent Application Publication No. 2007-0026441 A1 published February 1, 2007;

8. G.P. Allaway et al., U.S. Patent Application Publication No. 2002-0155429 published October 24, 2002;

9. February 15, 1996 Advisory Action in connection with U.S. Application Serial No. 08/169,311 (**Exhibit 1**);

10. September 13, 1995 Final Office Action in connection with U.S. Application Serial No. 08/169,311 (**Exhibit 2**);

11. November 23, 1994 Office Action in connection with U.S. Application Serial No. 08/169,311 (**Exhibit 3**);

12. August 18, 1994 Office Action in connection with U.S. Application Serial No. 08/169,311 (**Exhibit 4**);

13. July 16, 1998 Notice of Acceptance in connection with Australian Application No. 14387/95 (**Exhibit 5**);

14. November 27, 1996 Examiner's First Report in connection with Australian Application No. 14387/95 (**Exhibit 6**);

15. July 5, 2000 Notice of Acceptance in connection with Australian Application No. 62690/96 (**Exhibit 7**);

16. November 10, 1998 Examiner's First Report in connection with Australian Application No. 62690/96 (**Exhibit 8**);

17. September 14, 2006 Official Action in connection with Canadian Application No. 2,224,003 (**Exhibit 9**);

18. September 11, 2006 Communication Pursuant to Article 96(2) EPC in connection with European Application No. 96 921 473.3 (**Exhibit 10**);

19. March 8, 2006 Summons to Oral Proceedings Pursuant to Rule 71(1) EPC in connection with European Application No. 96 921 473.3 (**Exhibit 11**);

20. February 24, 2005 Provision of a Copy of the Minutes in accordance with Rule 76(4) EPC in connection with European Application No. 96 921 473.3 (**Exhibit 12**);

21. February 24, 2005 Decision to Refuse a European Patent Application in connection with European Application No. 96 921 473.3 (**Exhibit 13**);

22. August 30, 2004 Summons to Oral Proceedings Pursuant to Rule 71(1) EPC in connection with European Application No. 96 921 473.3 (**Exhibit 14**);

23. December 19, 2002 Communication Pursuant to Article 96(2) EPC in connection with European Application No. 96 921 473.3 (**Exhibit 15**);

24. July 6, 2001 Communication Pursuant to Article 96(2) EPC in connection with European Application No. 96 921 473.3 (**Exhibit 16**);

25. December 20, 1999 Notice of Allowance and Allowability in connection with U.S. Application Serial No. 08/973,601 (**Exhibit 17**);

26. August 3, 1999 Advisory Action in connection with U.S. Application Serial No. 08/973,601 (**Exhibit 18**);

27. March 25, 1999 Office Action in connection with U.S. Application Serial No. 08/973,601 (**Exhibit 19**);

28. June 24, 1998 Office Action in connection with U.S. Application Serial No. 08/973,601 (**Exhibit 20**);

29. January 11, 2005 Notice of Allowance and Allowability in connection with U.S. Application Serial No. 09/412,284 (**Exhibit 21**);

30. December 2, 2003 Final Office Action in connection with U.S. Application Serial No. 09/412,284 (**Exhibit 22**);

31. February 3, 2003 Office Action in connection with U.S. Application Serial No. 09/412,284 (**Exhibit 23**);

32. April 8, 2002 Advisory Action in connection with U.S. Application Serial No. 09/412,284 (**Exhibit 24**);

33. September 11, 2001 Final Office Action in connection with U.S. Application Serial No. 09/412,284 (**Exhibit 25**);

34. December 19, 2000 Office Action in connection with U.S. Application Serial No. 09/412,284 (**Exhibit 26**);

35. April 18, 2007 Office Action in connection with U.S. Application Serial No. 11/258,963 (**Exhibit 27**);

36. December 26, 2006 Office Action in connection with U.S. Application Serial No. 11/258,963 (**Exhibit 28**);

37. February 8, 2007 Office Action in connection with U.S. Application Serial No. 09/904,356 (**Exhibit 29**);

38. May 2, 2006 Final Office Action in connection with U.S. Application Serial No. 09/904,356 (**Exhibit 30**);

39. October 12, 2005 Office Action in connection with U.S. Application Serial No. 09/904,356 (**Exhibit 31**);

40. July 29, 2005 Advisory Action in connection with U.S. Application Serial No. 09/904,356 (**Exhibit 32**);

41. November 17, 2004 Final Office Action in connection with U.S. Application Serial No. 09/904,356 (**Exhibit 33**);

42. July 1, 2003 Office Action in connection with U.S. Application Serial No. 09/904,356 (**Exhibit 34**);

43. September 29, 2003 Advisory Action in connection with U.S. Application Serial No. 09/118,415 (**Exhibit 35**);

44. January 28, 2003 Final Office Action in connection with U.S. Application Serial No. 09/118,415 (**Exhibit 36**);

45. April 9, 2002 Office Action in connection with U.S. Application Serial No. 09/118,415 (**Exhibit 37**);

46. August 14, 2001 Advisory Action in connection with U.S. Application Serial No. 09/118,415 (**Exhibit 38**);

47. November 24, 2000 Final Office Action in connection with U.S. Application Serial No. 09/118,415 (**Exhibit 39**);

48. February 11, 2000 Office Action in connection with U.S. Application Serial No. 09/118,415 (**Exhibit 40**);

49. August 3, 2006 Notice of Allowance and Allowability in connection with U.S. Application Serial No. 09/891,062 (**Exhibit 41**);

50. July 17, 2006 Notice of Allowability in connection with U.S. Application Serial No. 09/891,062 (**Exhibit 42**);

51. May 18, 2006 Notice of Allowance and Allowability in connection with U.S. Application Serial No. 09/891,062 (**Exhibit 43**);

52. August 8, 2005 Office Action in connection with U.S. Application Serial No. 09/891,062 (**Exhibit 44**);

53. March 21, 2005 Office Action in connection with U.S. Application Serial No. 09/891,062 (**Exhibit 45**);

54. May 28, 2004 Advisory Action in connection with U.S. Application Serial No. 09/891,062 (**Exhibit 46**);

55. September 24, 2003 Final Office Action in connection with U.S. Application Serial No. 09/891,062 (**Exhibit 47**);

56. December 18, 2002 Office Action in connection with U.S. Application Serial No. 09/891,062 (**Exhibit 48**);

57. April 30, 2007 Notice of Allowance and Allowability in connection with U.S. Application Serial No. 11/544,346 (**Exhibit 49**);

58. March 3, 1997 Office Action in connection with U.S. Application Serial No. 08/627,684 (**Exhibit 50**);

59. June 23, 1997 Office Action in connection with U.S. Application Serial No. 08/663,616 (**Exhibit 51**);

60. March 13, 1997 Office Action in connection with U.S. Application Serial No. 08/673,682 (**Exhibit 52**);

61. November 28, 2000 Notice of Acceptance in connection with Australian Application No. 26074/97 (**Exhibit 53**);

62. July 13, 1999 Examiner's First Report in connection with Australian Application No. 26074/97 (**Exhibit 54**);

63. October 23, 2006 Official Action in connection with Canadian Application No. 2,250,829 (**Exhibit 55**);

64. May 27, 2005 Official Action in connection with Canadian Application No. 2,250,829 (**Exhibit 56**);

65. May 4, 2007 Summons to Attend Oral Proceedings Pursuant to Rule 71(1) EPC in connection with European Application No. 97917856.3 (**Exhibit 57**);

66. January 27, 2006 Communication Pursuant to Article 96(2) EPC in connection with European Application No. 97917856.3 (**Exhibit 58**);

67. October 21, 2005 Communication Pursuant to Article 115(2) EPC in connection with European Application No. 97917856.3 (**Exhibit 59**);

68. April 1, 2005 Communication Pursuant to Article 96(2) EPC in connection with European Application No. 97917856.3 (**Exhibit 60**);

69. August 5, 2004 Communication Pursuant to Article 96(2) EPC in connection with European Application No. 97917856.3 (**Exhibit 61**);

70. January 27, 2004 Communication Pursuant to Article 96(2) EPC in connection with European Application No. 97917856.3 (**Exhibit 62**);

71. May 9, 2003 Communication Pursuant to Article 96(2) EPC in connection with European Application No. 97917856.3 (**Exhibit 63**);

72. March 6, 2002 Search Report Communication in connection with European Application No. 97917856.3 (**Exhibit 64**);

73. February 27, 2007 Notification of Reasons for Rejection in connection with Japanese Application No. 535610/97 (English translation) (**Exhibit 65**);

74. May 19, 2006 Examiner's First Report in connection with Australian Application No. 2004233505 (**Exhibit 66**);

75. July 26, 2004 Notice of Acceptance in connection with Australian Application No. 35106/01 (**Exhibit 67**);

76. July 5, 2004 Examiner's Second Report in connection with Australian Application No. 35106/01 (**Exhibit 68**);

77. November 1, 2002 Examiner's First Report in connection with Australian Application No. 35106/01 (**Exhibit 69**);

78. December 4, 2001 Notice of Allowance and Allowability in connection with U.S. Application Serial No. 08/831,823 (**Exhibit 70**);

79. January 16, 2001 Notice of Allowance and Allowability in connection with U.S. Application Serial No. 08/831,823 (**Exhibit 71**);

80. September 26, 2000 Advisory Action in connection with U.S. Application Serial No. 08/831,823 (**Exhibit 72**);

81. April 11, 2000 Final Office Action in connection with U.S. Application Serial No. 08/831,823 (**Exhibit 73**);

82. July 21, 1999 Final Office Action in connection with U.S. Application Serial No. 08/831,823 (**Exhibit 74**);

83. December 21, 1998 Office Action in connection with U.S. Application Serial No. 08/831,823 (**Exhibit 75**);

84. August 17, 1998 Office Action in connection with U.S. Application Serial No. 08/831,823 (**Exhibit 76**);

85. June 15, 2006 Final Office Action in connection with U.S. Application Serial No. 09/888,938 (**Exhibit 77**);

86. September 7, 2005 Office Action in connection with U.S. Application Serial No. 09/888,938 (**Exhibit 78**);

87. August 4, 2004 Office Action in connection with U.S. Application Serial No. 09/888,938 (**Exhibit 79**);

88. May 5, 2004 Office Action in connection with U.S. Application Serial No. 09/888,938 (**Exhibit 80**);

89. June 22, 1999 Notice of Allowance and Allowability in connection with U.S. Application Serial No. 08/876,078 (**Exhibit 81**);

90. December 21, 1998 Final Office Action in connection with U.S. Application Serial No. 08/876,078 (**Exhibit 82**);

91. March 23, 1998 Office Action in connection with U.S. Application Serial No. 08/876,078 (**Exhibit 83**);

92. June 16, 2006 Communication Pursuant to Article 96(2) EPC in connection with European Application No. 98 931 261.6 (**Exhibit 84**);

93. June 17, 2005 Communication Pursuant to Article 96(2) EPC in connection with European Application No. 98 931 261.6 (**Exhibit 85**);

94. October 17, 2006 Final Office Action in connection with U.S. Application Serial No. 09/460,216 (**Exhibit 86**);

95. February 3, 2006 Office Action in connection with U.S. Application Serial No. 09/460,216 (**Exhibit 87**);

96. July 29, 2005 Advisory Action in connection with U.S. Application Serial No. 09/460,216 (**Exhibit 88**);

97. February 09, 2005 Final Office Action in connection with U.S. Application Serial No. 09/460,216 (**Exhibit 89**);

98. September 26, 2003 Advisory Action in connection with U.S. Application Serial No. 09/460,216 (**Exhibit 90**);

99. February 27, 2003 Final Office Action in connection with U.S. Application Serial No. 09/460,216 (**Exhibit 91**);

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111. September 23, 2004 Office Action in connection with U.S. Application Serial No. 09/724,105 (**Exhibit 103**);

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127. January 10, 2005 Communication Pursuant to Article 96(2) EPC in connection with European Application No. 99 966 466.7 (**Exhibit 119**);

128. October 14, 2004 Communication Pursuant to Article 96(1) and Rule 51(1) EPC in connection with European Application No. 99 966 466.7 (**Exhibit 120**);

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No fee, other than the $525.00 fee for a three-month extension of time and the $180.00 fee for filing a Supplemental Information Disclosure Statement, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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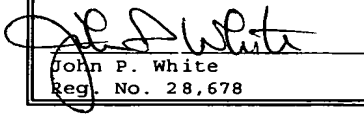

11/30/07
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